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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/729,799	12/05/2003	Itai Adin	225548	2262

23460 7590 06/20/2006

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EXAMINER	
QAZI, SABIHA NAIM	

ART UNIT	PAPER NUMBER
1616	

DATE MAILED: 06/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/729,799	ADIN ET AL.	
	Examiner	Art Unit	
	Sabiha Qazi	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 May 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Final Office Action

Acknowledgment is made of the Remarks and Amendments filed on 5/10//2006. Claims 28-43 are pending. No claim is allowed. Amendments are entered.

Presently claimed invention is drawn to trihalogenated halobetasol propionate, which is marketed in US as Ultravate cream and Ultravate ointment as anti-inflammatory agent. The reference KALVODA et al. US Patent 4,619,921 discloses this compound in crystalline form having m.p. 220-221 C.

The KALVODA patent and the Ultravate product belong to Bristol-Myers Squibb Company.

Data in The Specification

The examples in the specification, specifically Examples 14, 15, and 16 disclose halobetasol propionate at 0.05%, which is the *exact same* used by Bristol-Myers Squibb in their product, Ultravete. There is no crystalline form mentioned in these examples, so it is the same compound.

Response to Remarks

Applicant's arguments were fully considered, but are not found persuasive. Therefore, the rejection is maintained.

102(b) Rejection

KALVODA et al's Example 5 discloses crystalline halobetasol propionate. The compound was re-crystallized methylene chloride/ether. The Applicants arguments that their invention is novel because the melting points are different from KALVODA is not found persuasive. The Applicants' Crystalline Form II has a melting point of 214.5-215.0 degrees Celsius, which is close to KALVODA's 220-221 degrees Celsius. That difference is so small that it may be part of experimental conditions.

Applicants have not provided a comparison of KALVODA's crystalline compound and the instant invention. Even if KALVODA does not disclose the X-ray data, the property is inherent.

See Exparte Novitski, 26 USPQ 2d 1389 (January 22, 1993) which is decision of USPTO Board of Appeals, holding to be inherent and not patentable, inoculating healthy plants with a known plant inoculant's,

employed in the prior art to protect them against phytopathogenic fungi. Novitski discovered that the known plant inoculants would also protect them against root dwelling plant pathogenic nematodes, a discovery neither known nor appreciated by the prior art. The step of inoculating plants with the same inoculants necessarily and inherently protects them against nematodes.

See Atlas Powder versus Ireco, 51 USPQ 2d 1943, (Fed. Cir. 1999), holds the failure of those skilled in the art to contemporaneously recognize an inherent property, function, or ingredient of a prior art reference does not preclude a finding of anticipation. Whether or not an element is inherent in the prior art is a fact question. Inherency is not necessarily conterminous with knowledge of those of ordinary skill in the art, who may not recognize the inherent characteristics or functioning of the prior art. However the discovery of a previously unappreciated property of a prior art composition does not render the old composition new to the discoverer.

The fact that prior art taught away from the claim is, in fact, only a showing that prior art did not recognize the inherent function. This lack of contemporary understanding did not defeat the showing of inherency.

103(a) rejection

The Applicants argue that there is no motivation for one skilled in the art to have combined the teachings of KALVODA, BRITTAIN 1, and BRITTAIN 2 to render obvious crystalline forms of halobetasol propionate as recited in the claims.

The Examiner respectfully disagrees. ***BRITTAIN 1 and BRITTAIN 2 teach that compounds may be polymorphs (polymorphs = forms having the same chemical composition but different crystal structures).***

One skilled in the art would have already known this.

There is motivation for one skilled in the art to take the teachings of KALVODA and BRITTAIN 1 & 2 because KALVODA teaches halobetasol propionate and BRITTAIN teaches that compounds may have the same chemical composition but different crystal structures. Since the instant invention is the same chemical composition but a different crystal structure, the instant invention is *prima facie* obvious over KALVODA and BRITTAIN 1 & 2.

Claim Rejections - 35 USC § 102(b)

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> *A person shall be entitled to a patent unless –*
>
> *(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.*

Claims 28-36 are rejected under 35 U.S.C. 102(b) as being anticipated by KALVODA et al. (US Patent 4,619,921). See (1) in col. 1, compound (II) in col. 2, lines 38-41 in col. 6 and example 5. The resulting compositions are expected to be the same as disclosed by the reference.

In an event where the composition as claimed may have different use, the two different intended uses are not distinguishable in terms of the composition, see *In re Thuau,* 57 USPQ 324; *Ex parte Douros,* 163 USPQ 667; and *In re Craige,* 89 USPQ 393.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> *(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.*

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time

any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 28-43 are rejected under 35 U.S.C. 103(a) as being unpatentable over United States Patent No. 4,619921, Brittain, H.G., (polymorphism in pharmaceutical solid, Drugs and the pharmaceutical sciences, vol. 95, 1999, chapter 6, pages 227-240; reference 1) and Brittain, H.G., (polymorphism in pharmaceutical solid, Drugs and the pharmaceutical sciences, vol. 95, 1999, chapter 6, pages 348-361; reference 2). See the entire documents.

Presently claimed invention is drawn to trihalogenated halobetasol propionate, which is marketed in US as Ultravate cream and Ultravate ointment as anti-inflammatory agent by Bristol-Myers Squibb Company. The reference KALVODA et al. US Patent 4,619,921 discloses this compound in crystalline form having m.p. 220-221 C.

Brittain teaches (ref. 1) that compounds may be polymorphs i.e. forms having the same chemical composition but different crystal structures (introduction on page 228). See also fig. 1 on page 233. Different X-ray powder diffraction pattern is observed for each suspected polymorphic variation. See also X-ray Powder diffraction on page 235 where the technique of X-powder diffraction is disclosed as predominant tool for the study of polycrystalline materials and is eminently suited for routine characterization of polymorphs and solvates. The X-ray diffraction will therefore consist of a series of peaks detected as characteristic scattering angles. See page 236, first paragraph.

Brittain also teaches (ref. 2) changes in crystal forms affected by compaction and exemplified by applying to various useful drugs. See the entire document. See also fig. 7 on page 349 and figure 8 on page 352.

It would have been obvious to one skilled in the art to prepare various polymorphs of the known drug halobatasol because process of making polymorphs are known by various methods as cited in Brittain references. Different polymorphs are expected for a given compound, which would result in different X-ray powder diffraction pattern. One would have been motivated to prepare instantly claimed invention since it has long been the practice in the chemical and pharmaceutical arts to produce compounds in the form of crystals in pure form and may have different polymorphic forms. Changing the physical form, purity, enhanced deliverability etc of an old product does

not render the compound or the composition patentable because the difference in physical forms, purity etc was inherent in or rendered obvious by the prior art. See In re Cofer, 148 U.S.P.Q. 268 (CCPA) 1966). Some polymorphic forms may be more stable than the other depending on arrangements of atoms. One of the skilled in the art would have been motivated to prepare different crystalline e forms of known pharmaceutically useful compounds with the expectation of obtaining useful benefits such as longer shelf life, stability, enhanced deliverability, etc.

In absence of a showing of a viable unexpected property not only the X-ray diffraction pattern or stability, which are obvious to one skilled in the art, presently claimed invention of various forms of polymorphs and composition of a known compound halobetasol propionate and its X-diffractions would have been *prima facie* obvious to one skilled in the art. Furthermore, that one skilled in the art would know process of purification by crystallization of a compound because crystallization is a empirical skill well taught and recognized in the chemical art as is clear from the teachings by Brittain references cited above.

It has been decided by the courts that even in a case where the reference does not teach the same use of the composition, the two different intended uses are not distinguishable in terms of the composition, see *In re Thuau,* 57 USPQ 324; *Ex parte Douros,* 163 USPQ 667; and *In re Craige,* 89 USPQ 393.

Also, Applicants have not provided a side-by-side comparison of KALVODA's crystalline compound and the instant invention. Even if KALVODA does not disclose the X-ray data, the property is inherent. See Exparte Novitski, 26 USPQ 2d 1389 (January 22, 1993) which is decision of USPTO Board of Appeals, holding to be inherent and not patentable, inoculating healthy plants with a known plant inoculant's, employed in the prior art to protect them against phytopathogenic fungi. Novitski discovered that the known plant inoculants would also protect them against root dwelling plant pathogenic nematodes, a discovery neither known nor appreciated by the prior art. The step of inoculating plants with the same inoculants necessarily and inherently protects them against nematodes.

See Atlas Powder versus Ireco, 51 USPQ 2d 1943, (Fed. Cir. 1999), holds the failure of those skilled in the art to contemporaneously recognize an inherent property, function, or ingredient of a prior art reference does not preclude a finding of anticipation. Whether or not an element is inherent in the prior art is a fact question. Inherency is not necessarily conterminous with knowledge of those of ordinary skill in the art, who may not recognize the

inherent characteristics or functioning of the prior art. However the discovery of a previously unappreciated property of a prior art composition does not render the old composition new to the discoverer.

The fact that prior art taught away from the claim is, in fact, only a showing that prior art did not recognize the inherent function. This lack of contemporary understanding did not defeat the showing of inherency.

In the light of the forgoing discussion, the Examiner's ultimate legal conclusion is that the subject matter defined by the instant claims would have been obvious within the meaning of 35 U.S.C. 103(a).

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Communication

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sabiha Qazi, Ph.D. whose telephone number is 571-272-0622. The examiner can normally be reached on any business day.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's acting supervisor, Johann Richter, Ph.D. can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sunday
June 11 2006

SABIHA QAZI, PH.D
PRIMARY EXAMINER